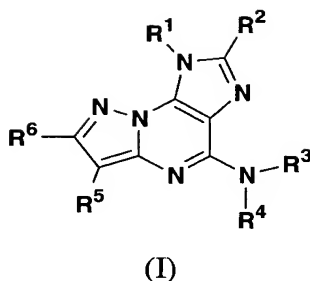


We claim:

1. A compound of formula (I),



enantiomers, diastereomers, salts, and solvates thereof wherein

R¹ is

- (a) hydrogen, or
- (b) alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z¹, Z² and Z³;

R² is

- (a) hydrogen, halo, cyano,
- (b) alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, cycloalkoxy, heterocyclooxy, aryloxy, heteroaryloxy, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1a}, Z^{2a} and Z^{3a}; or
- (c) -OR^{10a}, -SR^{10a}, or -SO₂R^{10a}

R³ and R⁴ are independently

- (a) hydrogen,
- (b) alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which

may be optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b} and Z^{3b} ;

- (c) $-OR^{11}$, $-NR^{12}R^{13}$, $-N(R^{12})C(O)R^{11}$, $-N(R^{12})C(O)OR^{11}$, $-N(R^{12})SO_2R^{14}$, or $-C(O)NR^{12}R^{13}$, $-SO_2NR^{12}R^{13}$, $-N(R^{12})C(O)NR^{12a}R^{13}$, or $-N(R^{12})SO_2NR^{12a}R^{13}$; or
- 5 (d) R^3 and R^4 together with the nitrogen atom to which they are attached combine to form a heterocyclo ring optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b} and Z^{3b} ;

R^5 is

- (a) hydrogen, halo, hydroxy, cyano,
- 10 (b) alkyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1c} , Z^{2c} and Z^{3c} ; or
- (c) $-OR^7$, $-C(O)R^7$, $-C(O)OR^7$, or $-NR^8R^9$;

15 R^6 is

- (a) hydrogen, hydroxy, halo, or cyano,
- (b) alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclo, aryl, heteroaryl, (cycloalkyl)alkyl, (heterocyclo)alkyl, (aryl)alkyl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one
- 20 or more Z^{1d} , Z^{2d} and Z^{3d} ; or
- (c) $-OR^{7a}$, $-NR^{8a}R^{9a}$, $-N(R^{8a})SO_2R^{10}$, $-N(R^{8a})SO_2NR^{8b}R^{9b}$, $-N(R^{8a})C(O)R^{7a}$, $-N(R^{8a})C(O)NR^{8b}R^{9b}$, $-N(R^{8a})C(O)OR^{7a}$, $-C(O)R^{7a}$, $-C(O)OR^{7a}$, $-OC(O)R^{7a}$, $-C(O)NR^{8a}R^{9a}$, or $-OC(O)NR^{8a}R^{9a}$;

R^7 , R^{7a} and R^{7b} are independently

- 25 (a) hydrogen, or
- (b) alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1c} , Z^{2c} and Z^{3c} ;

30 R^8 , R^{8a} , R^{8b} , R^9 , R^{9a} and R^{9b} are independently

(a) hydrogen,

(b) alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1d} , Z^{2d} and Z^{3d} ; or

(c) $-OR^{7b}$, $-NR^{8c}R^{9c}$, $-N(R^{8c})SO_2R^{10b}$, $-N(R^{8c})C(O)R^{7b}$, $-N(R^{8c})C(O)OR^{7b}$, $-SO_2NR^{8c}R^{9c}$, $-SO_2R^{10b}$, $-C(O)R^{7b}$, $-C(O)OR^{7b}$, or $-C(O)NR^{8c}R^{9c}$;

R^{8c} and R^{9c} are independently

(a) hydrogen,

(b) alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1d} , Z^{2d} and Z^{3d} ;

R^{10} , R^{10a} and R^{10b} are independently alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl,

(cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1d} , Z^{2d} and Z^{3d} ;

R^{11} , R^{12} , R^{12a} and R^{13} are independently

(a) hydrogen, or

(b) alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1e} , Z^{2e} and Z^{3e} ;

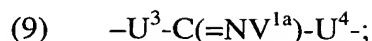
R^{14} is alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl,

heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1e} , Z^{2e} and Z^{3e} ;

Z^{1-1e} , Z^{2-2e} , and Z^{3-3e} are optional substituents independently selected from

(1) Y, where Y is

- (i) alkyl, (hydroxy)alkyl, (alkoxy)alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl;
- 5 (ii) a group (i) which is itself substituted by one or more of the same or different groups (i); or
- (iii) a group (i) or (ii) which is independently substituted by one or more (preferably 1 to 3) of the following groups (2) to (13) of the definition of Z^1 ,
- 10 (2) $-OH$ or $-OY^1$,
- (3) $-SH$ or $-SY^1$,
- (4) $-C(O)_tH$, $-C(O)_tY^1$, or $-O-C(O)Y^1$, where t is 1 or 2,
- (5) $-SO_3H$, or $-S(O)_tY^1$,
- (6) halo,
- 15 (7) cyano,
- (8) nitro,
- (9) $-U^1-NY^2Y^3$,
- (10) $-U^1-N(Y^1)-U^2-NY^2Y^3$,
- (11) $-U^1-N(Y^4)-U^2-Y^1$,
- 20 (12) $-U^1-N(Y^4)-U^2-H$,
- (13) oxo;
- U^1 and U^2 are each independently
- (1) a single bond,
- (2) $-U^3-S(O)_t-U^4-$,
- 25 (3) $-U^3-C(O)-U^4-$,
- (4) $-U^3-C(S)-U^4-$,
- (5) $-U^3-O-U^4-$,
- (6) $-U^3-S-U^4-$,
- (7) $-U^3-O-C(O)-U^4-$,
- 30 (8) $-U^3-C(O)-O-U^4-$, or



V^{1a} is independently hydrogen, alkyl, -CN, -C(O)Y¹, -S(O)₂Y⁵, S(O)₂NY²Y³;

Y¹, Y², Y³ and Y⁴

(1) are each independently hydrogen or a group provided in

- 5 (i) alkyl, (hydroxy)alkyl, (alkoxy)alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl;
- (ii) a group (i) which is itself substituted by one or more of the
- 10 same or different groups (i),
- (iii) a group (i) or (ii) which is independently substituted by one or more (preferably 1 to 3) of the following groups (1) to (12) of the definition of Z⁴, or

(2) Y² and Y³ may together be alkylene or alkenylene, completing a 3- to 8-

15 membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with one or more groups selected from alkyl, (hydroxy)alkyl, (alkoxy)alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl,

20 or

(3) Y² or Y³, together with Y¹, may be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more groups selected from alkyl, (hydroxy)alkyl, (alkoxy)alkyl, alkenyl,

25 alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl, or

(4) Y² and Y³ together with the nitrogen atom to which they are attached may combine to form a group -N=CY⁵Y⁶ where Y⁵ and Y⁶ are each independently

30 H or a group provided selected from alkyl, (hydroxy)alkyl, (alkoxy)alkyl,

alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl,
 (cycloalkenyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl,
 heteroaryl, or (heteroaryl)alkyl; and

Z⁴ is

- 5 (1) -OH or -OY^a,
- (2) -SH or -SY^a,
- (3) -C(O)_tH, -C(O)_tY^a, or -O-C(O)Y^a, where t is 1 or 2,
- (4) -SO₃H, or -S(O)_tY^a,
- (5) halo,
- 10 (6) cyano,
- (7) nitro,
- (8) -U¹-NY^bY^c,
- (9) -U¹-N(Y¹)-U²-NY^bY^c,
- (10) -U¹-N(Y^d)-U²-Y^a,
- 15 (11) -U¹-N(Y^d)-U²-H,
- (12) oxo;

Y^a, Y^b, Y^c and Y^d

(1) are each independently hydrogen or a group provided in

- (i) alkyl, (hydroxy)alkyl, (alkoxy)alkyl, alkenyl, alkynyl,
 20 cycloalkyl, (cycloalkyl)alkyl, cycloalkenyl, (cycloalkenyl)alkyl,
 aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or
 (heteroaryl)alkyl;

U³ and U⁴ are each independently

- (1) a single bond,
- 25 (2) alkylene,
- (3) alkenylene, or
- (4) alkynylene.

2. A compound of claim 1 wherein

30 R³ and R⁴ are independently

- (a) hydrogen,
- (b) alkyl, haloalkyl, (hydroxy)alkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, (aryl)alkyl or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b} and Z^{3b} ; or
- (c) R^3 and R^4 together with the nitrogen atom to which they are attached combine to form a heterocyclo ring optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b} and Z^{3b} .
3. A compound of claim 2 wherein R^6 is
- (a) alkyl, alkenyl, alkynyl, heteroaryl or aryl any of which may be optionally independently substituted as valence allows with one or more Z^{1d} , Z^{2d} and Z^{3d} ; or
- (b) $-OR^{7a}$.
4. A compound of claim 3 wherein R^{7a} is alkyl optionally substituted with Z^{1c} .
5. A compound of claim 4 wherein Z^{1b} , Z^{2b} and Z^{3b} are optional substituents independently selected from $-OH$, $-OY^1$, $-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-N(Y^1)-U^2-NY^2Y^3$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$; Z^{1c} is
- (a) $-OH$, $-OY^1$ or
- (b) aryl optionally substituted with $-OH$ or $-OY^1$;
- Z^{1d} , Z^{2d} and Z^{3d} are optional substituents independently selected from
- (a) cyano, halo, $-OH$, $-OY^1$, $-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-S(O)_tY^1$, $-N(Y^1)-U^2-NY^2Y^3$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$;
- (b) alkyl or alkoxy optionally substituted with one or more cyano, halo, $-OH$, $-OY^1$, $-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-S(O)_tY^1$, $-N(Y^1)-U^2-NY^2Y^3$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$.

6. A compound of of claim 5 wherein

R³ is hydrogen;

R⁴ is alkyl, haloalkyl, (hydroxy)alkyl, cycloalkyl, (cycloalkyl)alkyl, heterocyclo,

5 (heterocyclo)alkyl, (aryl)alkyl or (heteroaryl)alkyl any of which may be optionally independently substituted as valence allows with one or more Z^{1b}, Z^{2b} and Z^{3b};

R⁶ is

(a) alkynyl optionally substituted with Z^{1d} where Z^{1d} is aryl which may be further optionally independently substituted with one or more cyano, halo, -OH, -OY¹,

10 -U¹-NY²Y³, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, -N(Y¹)-U²-NY²Y³, -N(Y⁴)-U²-Y¹, or -N(Y⁴)-U²-H;

(b) aryl optionally independently substituted as valence allows with one or more Z^{1d}, Z^{2d} and Z^{3d};

(c) -OR^{7a}; or

15 (d) heterocyclo optionally independently substituted as valence allows with one or more Z^{1d}, Z^{2d} and Z^{3d};

Z^{1b}, Z^{2b} and Z^{3b} are optional substituents independently selected from -OH, -OY¹, -U¹-NY²Y³, -C(O)_tH, -C(O)_tY¹, -N(Y⁴)-U²-Y, or -N(Y⁴)-U²-H

where

20 U¹ is a bond,

U² is -U³-C(O)-U⁴- or -U³-C(O)O-U⁴- and

U³ and U⁴ are independently a bond or alkylene ;

Z^{1c} is

(a) -OY¹ where Y¹ is aryl, or

25 (b) aryl optionally substituted with -OH or -OY¹ where Y¹ is alkyl;

Z^{1d}, Z^{2d} and Z^{3d} are optional substituents independently selected from

(a) cyano, halo, -OH, -OY¹, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, or

(b) alkyl or alkoxy optionally substituted with one or more cyano, halo, -OH, -OY¹, -U¹-NY²Y³, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, -N(Y⁴)-U²-Y¹, or -N(Y⁴)-U²-H

30 where

U^1 is a bond, or $-C(O)-$,

U^2 is $-U^3-C(O)-U^4-$, $-U^3-C(O)O-U^4-$, or $-U^3-SO_2-U^4-$, and

U^3 and U^4 are independently a bond or alkylene.

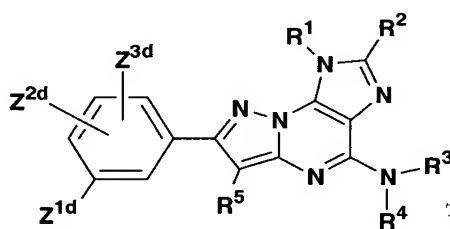
5 7. A compound of claim 6 wherein

R^1 is alkyl;

R^2 is hydrogen; and

R^5 is hydrogen or alkyl.

10 8. A compound of claim one having the formula IIa



IIa

wherein

Z^{1d} is

15 (a) cyano, halo, $-OH$, $-OY^1$, $-C(O)_tH$, $-C(O)_tY^1$, $-S(O)_tY^1$, or

(b) alkyl or alkoxy optionally substituted with one or more cyano, halo, $-OH$, $-OY^1$,
 $-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-S(O)_tY^1$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$

where

U^1 is a bond, or $-C(O)-$,

20 U^2 is $-U^3-C(O)-U^4-$, $-U^3-C(O)O-U^4-$, or $-U^3-SO_2-U^4-$, and

U^3 and U^4 are independently a bond or alkylene; and

Z^{2d} and Z^{3d} are optional substituents independently selected from

(a) cyano, halo, $-OH$, $-OY^1$, $-C(O)_tH$, $-C(O)_tY^1$, $-S(O)_tY^1$, or

(b) alkyl or alkoxy optionally substituted with one or more cyano, halo, $-OH$, $-OY^1$,
 25 $-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-S(O)_tY^1$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$

where

U^1 is a bond, or $-C(O)-$,

U^2 is $-U^3-C(O)-U^4-$, $-U^3-C(O)O-U^4-$, or $-U^3-SO_2-U^4-$, and

U^3 and U^4 are independently a bond or alkylene.

5 9. A compound of claim 8 wherein

R^3 and R^4 are independently

(a) hydrogen,

(b) alkyl, haloalkyl, (hydroxy)alkyl, cycloalkyl, (cycloalkyl)alkyl,

(heterocyclo)alkyl, (aryl)alkyl or (heteroaryl)alkyl and of which may be

10 optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b} and Z^{3b} ; or

(c) R^3 and R^4 together with the nitrogen atom to which they are attached combine to form a heterocyclo ring optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b} and Z^{3b} .

15

10. A compound of claim 9 wherein

Z^{1b} , Z^{2b} and Z^{3b} are optional substituents independently selected from $-OH$, $-OY^1$,

$-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-N(Y^1)-U^2-NY^2Y^3$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$.

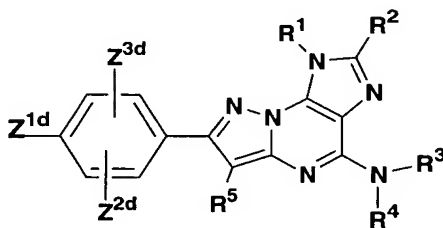
20 11. A compound of claim 10 wherein

R^1 is alkyl;

R^2 is hydrogen; and

R^5 is hydrogen or alkyl.

25 12. A compound of claim 1 having formula IIb



IIb

wherein

Z^{1d} is

(a) cyano, halo, -OH, -OY¹, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, or

5 (b) alkyl or alkoxy optionally substituted with one or more cyano, halo, -OH, -OY¹,
-U¹-NY²Y³, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, -N(Y⁴)-U²-Y¹, or -N(Y⁴)-U²-H

where

U¹ is a bond, or -C(O)-,

U² is -U³-C(O)-U⁴-, -U³-C(O)O-U⁴-, or -U³-SO₂-U⁴-, and

10 U³ and U⁴ are independently a bond or alkylene; and

Z^{2d} and Z^{3d} are optional substituents independently selected from

(a) cyano, halo, -OH, -OY¹, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, or

(b) alkyl or alkoxy optionally substituted with one or more cyano, halo, -OH, -OY¹,
-U¹-NY²Y³, -C(O)_tH, -C(O)_tY¹, -S(O)_tY¹, -N(Y⁴)-U²-Y¹, or -N(Y⁴)-U²-H

15 where

U¹ is a bond, or -C(O)-,

U² is -U³-C(O)-U⁴-, -U³-C(O)O-U⁴-, or -U³-SO₂-U⁴-, and

U³ and U⁴ are independently a bond or alkylene.

20

13. A compound of claim 12 wherein

R^3 and R^4 are independently

(a) hydrogen,

(b) alkyl, haloalkyl, (hydroxy)alkyl, cycloalkyl, (cycloalkyl)alkyl,

25 (heterocyclo)alkyl, (aryl)alkyl or (heteroaryl)alkyl and of which may be
optionally independently substituted as valence allows with one or more Z^{1b} , Z^{2b}
and Z^{3b} ; or

(c) R^3 and R^4 together with the nitrogen atom to which they are attached combine to
form a heterocyclo ring optionally independently substituted as valence allows
30 with one or more Z^{1b} , Z^{2b} and Z^{3b} .

14. A compound of claim 13 wherein

Z^{1b} , Z^{2b} and Z^{3b} are optional substituents independently selected from $-OH$, $-OY^1$,
 $-U^1-NY^2Y^3$, $-C(O)_tH$, $-C(O)_tY^1$, $-N(Y^1)-U^2-NY^2Y^3$, $-N(Y^4)-U^2-Y^1$, or $-N(Y^4)-U^2-H$.

5

15. A compound of claim 14 wherein

R^1 is alkyl;

R^2 is hydrogen; and

R^5 is hydrogen or alkyl.

10

16. A pharmaceutical composition comprising (a) at least one compound according to claim 1, or a pharmaceutically acceptable salt, hydrate or prodrug thereof, and (b) a pharmaceutically-acceptable carrier or diluent.

15 17. A method of treating an inflammatory or immune disease or disorder comprising administering to a mammal in need thereof a therapeutically-effective amount of at least one compound according to claim 1.

18. The method of claim 17 in which the inflammatory or immune disease is selected
20 from rheumatoid arthritis, asthma, inflammatory bowel disease, chronic obstructive pulmonary disease, and psoriasis.

19. A method of treating cancer comprising administering to a mammal in need thereof a therapeutically-effective amount of at least one compound according to claim

25 15.